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PROCESS AND DEVICE FOR EXAMINING CHEMICAL REACTIONS IN MINIATURIZED REACTORS ARRANGED PARALLEL TO EACH OTHER

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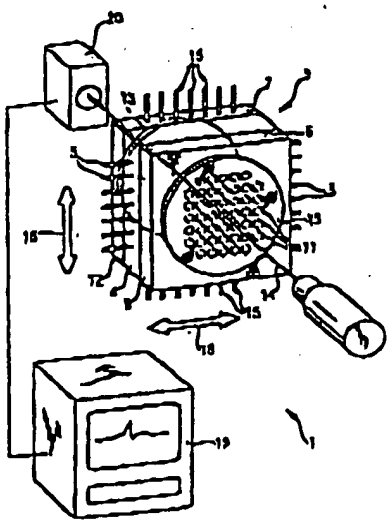
Abstract

The invention pertains to a process for examining chemical reactions in the presence of potentially catalytical substance, wherein reactions are triggered in miniaturized reactors arranged parallel to each other and the nature and amount of the reaction mixture are analyzed during the reaction time. A facility involving reactors provided with inlet pipes and by-passes has miniaturized reactors with volumes of 0,001 cm^3 to 1 cm^3. Said invention allows for effecting a large number of reactions under virtually identical conditions and with a relatively low amount of substance and samples, at an attractive cost and in a reproducible manner, and simultaneous spectroscopic analysis. It also provides a means of using for industrial catalyst screening the possibilities discussed in relation to combinatorial chemistry. Choosing identical samples and other different reaction conditions ensures optimized parallel reactions.



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Description

A process and device for investigating chemical reactions in miniaturized reactors connected in parallel.

The invention concerns a process for the investigation of chemical reactions in the presence of potentially catalytic substances, where the reactions are carried out in parallel in reactors. The invention additionally concerns a device, in particular for conducting this process, where the device has several reactors connected in parallel, which are provided with supply and discharge connections.

Processes and devices of this kind are known and are used, among other ways, in the search for catalysts for heterogeneous or homogeneous catalysis of industrial chemical processes.

Recently, however, new techniques are making it possible to prepare substances, that may be potential catalysts for a vast number of chemical processes in large numbers (P. G. Schultz et al., Science 1995, 1738). The investigation of this large number of potential catalysts is hardly possible any more with the traditional serial screening processes, since these screening processes are limited with regard to throughput and analytical resolving power as well as in their reproducibility. Frequently for a pure activity screening, completely insufficient integral effects like heating of the catalysts, etc., are employed without direct product mixture or effectivity analysis. In addition, optimization of the conditions for catalyst activation and process conduct puts special requirements on quantitative analytical processes and on the reproducibility of the reaction conditions.

The invention thus was based on the task of developing a cost-favorable process or a cost-favorable device with which a large number of chemical reactions can be investigated in a short time ,and in doing so, reproducible qualitative and quantitative data regarding the composition of the various reaction mixtures and reaction products can be obtained.

This task is solved by a process of the kind mentioned at the start, which is characterized by the fact that the reactions are carried out in miniaturized reactors and the reaction mixture or the reaction products are analyzed according to kind and amount during the reaction time.

The task is additionally solved by a device of the said kind, which is characterized by the fact that the reactors are miniaturized, with a volume in the range of 0.001 cm^3 to 1 cm^3.

The object of the invention is therefore a process for investigation of chemical reactions in the presence of potentially catalytic substances, in which the reactions are carried out in parallel in reactors, which is characterized by the fact that the reactions are carried out in miniaturized reactors and the reaction mixture is analyzed according to kind and amount during the reaction time.

Another object of the invention is a device, in particular for carrying out this process, where the device has several reactors connected in parallel, which are provided with supply and discharge connections, which is characterized by the fact that the reactors are miniaturized, with a volume in the range of 0.001 cm^3 to 1 cm^3.

Particular developments or embodiments of the invention follow from the relevant subclaims. Individual characteristics or more than one of the individual characteristics mentioned in the

Claims can in each case on its own represent solutions in accordance with the invention, and the characteristics within the claim categories can also be combined in any way.

A particular form of development of the process in accordance with the invention is characterized by the fact that the reaction educts are continuously supplied to the reactors and the reaction products are removed continuously from the reactors. The batch method of processing is, however, likewise possible.

Another particular development form is characterized by the fact that one uses educts that are at least partly labeled with isotopes, preferably with deuterium (^{2}H) or heavy oxygen (^{18}O) or heavy carbon (^{13}C) or mixtures thereof. These generate characteristic spectral shifts in rotational vibration spectra, which besides labeling the reaction path through variations in the educt mixture can lead to new interesting reactions or reaction products and systematically contrasts smaller amounts of byproducts.

Different educt mixtures can also be supplied to individual reactors or to reactors connected into groups in order to detect or reveal synergies that may be present by using the methods of combinatorial chemistry.

The educt, reaction or product mixtures can be analyzed by means of spectroscopic analysis, preferably by means of infrared spectroscopy (IR), especially preferably with Fourier IR spectroscopy, at any desired point of time in the course of the reaction according to kind and amount of substances that they contain. Other spectroscopic methods such as laser or UV spectroscopy are likewise suitable for investigation. The process can be carried out at various temperatures and pressures, at temperatures in the range from -50°C to 600°C inclusive,

preferably from room temperature to 500°C, or at various pressures, at absolute pressures of 10^{-3} to 10^{3} bar, preferably of 10^{-2} to 200 bar. The data obtained can then be sent to a comprehensive parameter and data analysis.

The invention is additionally characterized by the fact that the reactions can be carried out in the presence of a heterogeneous or homogeneous catalyst and that the screening of the catalytic activity (i.e., product detection) and selectivity (main product distribution) of amounts of catalysts smaller than 10 mg, preferably smaller than 1 mg, is possible in one reactor.

In a particular embodiment of the device in accordance with the invention several miniaturized reactors that are separate from each other can be arranged in one block. The volume of this reactor can be in the range of 0.001 cm^3 to 1 cm^3, preferably from 0.01 cm^3 to 0.5 cm^3, especially preferably from 0.05 cm^3 to 0.2 cm^3. In another preferred embodiment of the device in accordance with the invention the reactors are arranged as a square or rectangular pattern in a metal block, which can be a rectangular parallelepiped or cube. The metal block can be provided with a heating block or cooling elements and can be connected to a temperature sensor in the vicinity of each individual reactor. This enables a controlled and reproducible temperature conduct. In this way, for example, a defined temperature gradient can be established through the metal block. The reactors are advantageously arranged in the same plane, which lies parallel to one surface of the cuboid. The supply and discharge connections of the individual reactors advantageously lie at least partly perpendicular to this plane. They can be realized in the metal block as through-holes. The reactors can be realized as drillings. The number of reactors in one block can be

more than 20, preferably more than 40, especially preferably more than 100, really especially preferably more than 200. With these reactors small amounts of potential catalysts (also called samples below) can, under defined reaction conditions, be brought into contact and reacted, discontinuously or continuously, in parallel, i.e., simultaneously with an educt or educt mixtures in liquid and/or gaseous form. Automation of the device in accordance with the invention is possible, in particular the coating of the reactors with catalysts can be done automatically, preferably by a laboratory robot or pipetting device.

In another particular embodiment the miniaturized reactors are realized in the metal block as 4 mm drillings and are arranged so that various educt and inert gases can be made to flow through them through 2.5-mm capillary drillings. The gases then go to a spacer, preferably a spacer plate, which is affixed on the metal block and in which the drillings of the metal block continue. The arrangement of metal block and spacer is provided with a conventional cuvette drilling, in which the gases can be spectroscopically analyzed. For this the drilling is sealed at both ends with a transparent window. If one wishes to use infrared spectroscopy for the analysis, one preferably uses windows of 1-1-1 silicon, NaCl, Kbr, Ge, ZnSe or KSR5. For the analysis a collimated analysis beam, an infrared beam in the case of IR spectroscopy, is directed, preferably glare-free from an interferometer-coupled and dry gas-flushed space through the cuvette drilling, to a detector situated beyond it. The cuvette drilling can be, for example, 5 mm in size. By the choice of a suitable thick spacer the length of the cuvette drilling can be chosen to be between a few centimeters (1-10) and several tens of centimeters (10-50), in each case according to reaction

conditions and reaction type. For acquisition of the spectra the analysis beam can be directed through all of the cuvette drillings successively with the aid of a deflector. Several beams or several analyzers can also be used, so that simultaneous acquisition of spectra with several reactors is possible. Likewise, the block with the reactors can also be rotated with the aid of rotation devices, for example step motors, so that all of the cuvette drillings are brought into the optical path of the spectrometer in succession. As materials for the block and spacer preferably the common corrosion-resistant metal materials that are familiar to the expert, especially aluminum or steel, preferably rust- and/or acid- and/or high-temperature-resistant, are suitable.

Another embodiment of the device in accordance with the invention, which is particularly suitable for homogeneous catalysis, is characterized by the fact that in the case of at least one reactor with a volume which is preferably less than 200 µL, an ATR crystal (ATR = attenuated total reflection spectroscopy), preferably conically pointed, preferably made of ZnSe or of KSR5 or of diamond) enables spectroscopic contact to the reaction mixture for various solvents and reaction conditions and pressures up to 200 bar. In this case the analysis beam is focused on the ATR crystal.

The advantages of the process in accordance with the invention and the device in accordance in accordance with the invention lie essentially in the fact that a large number of reactions can be carried out, under practically identical conditions and with comparably small amounts of materials and samples, rapidly, cost effectively and reproducibly and at the same time can be investigated spectroscopically. It thus offers

the capability of using the capabilities that have been discussed in connection with combinatorial chemistry (K. Burgess et al., Ang. Chem., 1996, 108, 2, 192, integrated into the application by reference) for an industrial catalyst screening. By the choice of identical samples and various other reaction conditions like temperature, pressure, educt composition is possible to carry out a parallel reaction optimization.

For analysis of the obtained data it is advantageous to set up a data matrix in such a way that all selectable and documentable reaction conditions (educt partial pressures, educt composition, temperature, flow or flow rate, total pressure, sample composition, sample lattice constant and all supporting positions of the spectra) are represented according to reaction conditions, i.e., per reactor, as columns of the matrix. This matrix can undergo a factor analysis (E. R. Malinowski et al., Factor Analysis in Chemistry, Wiley, New York, 1980, integrated into the application by reference), by calculating the covariance matrix, the characteristic values, the abstract characteristic vectors, the loadings as well as the multidimensional regression coefficients and outputting it preferably as data files. A (pre)normalization of the data through the average value "0" and standard deviations "1" can also be chosen, whereby baselines and absolute value effects can be avoided. This allows the prediction of various quantities from the calibration data records (such as, for example, quantitative CO_2 amounts at various temperatures), the determination of the dependency of parameters in spectral ranges for optimization of the analysis, the generation of various distance matrixes from the starting data (for example, the similarity of catalysts with respect to the selected quantities and properties) and direct feedback of the catalyst

composition to a synthesis laboratory robot, which mixes a set of new catalyst samples and synthesizes it on a new robot line "by itself" by sintering or calcining.

Below a development form of the process in accordance with the invention and an embodiment of the device in accordance with the invention are illustrated more closely by means of Figures 1 and 2, without this having any intention of limiting the invention in any way.

Figure 1 shows a schematic representation of the device 1 in accordance with the invention in the optical path of a spectroscopic analyzer;

Figure 2 shows an individual reactor 2 from the device 1 in accordance with the invention in a sectional side view.

A device 1 for investigation of chemical reactions consists essentially of a block-shaped arrangement 3 of miniaturized reactors 2. The block-shaped arrangement 3 is realized so that the reactors 2 are incorporated in the form of drillings in a cuboid metal block 4, which has a front side 6 and a back side 7. The reactors 2 are drilled into the front side 6 of the cuboid metal block 4 and arranged in a rectangular pattern. They are connected with drillings 5 for supply of the educt. Catalysts 8 are introduced into the reactors 2. A spacer plate 9 is put on the front side 6 as a spacer, into which the reactors 2 continue as drillings. From these additional drillings 10, which serve for withdrawal of the reaction products, lead to a cuvette drilling 11. A spacer plate 12 is put on the back side 7 as another spacer. The cuvette drilling 11 continues through the metal block 4 and through the spacer plate 12. It is covered with transparent windows 13 on the free surfaces of the spacer plates and serves for withdrawal of the reaction products and at the same time as a

space for their spectroscopic analysis by means of an IR beam 14. The reaction products coming from reactor 2 are directed through the drillings 10 and 11 in correspondence with the arrows. From the end of the cuvette drilling 11 in spacer plate 12 they are removed via drillings 15. In the vicinity of reactors 2 there are heating elements 17 and thermocouples 18 in metal block 4. The block shaped arrangement 3 is rotatable by step motors 16 in both spatial directions perpendicular to IR beam 14. In this way each of the cuvette drillings 11 belonging to one of the reactors 2 can be rotated into the IR beam. The analysis of the IR beam takes place by recording the interferogram with the aid of interferometer 20 and detector 19, which are arranged near the transparent windows 13.

A test example with a known analyzer is described below.

In the device in accordance with the invention, various substances with a mixture of 30.2% by volume propylene 2.5, 15.2% by volume oxygen 4.5, with the remainder being nitrogen 5.0 were put into the reactors of the reactor block. One of the reactors contained a small amount (5 mg) of a known industrial catalyst for oxidation of propylene to acrolein. The IR spectra of all the reaction gases were fully automatically recorded at various temperatures. Figure 3 shows the spectrum of the reaction gas of the reactor, which contained the known catalyst at 400 and 450°C. At 400°C the product (acrolein from oxygen and propylene) can already be detected. However, a large amount of carbon dioxide still was produced. At 450°C no more carbon dioxide was established, and the product yield had increased. (The light negative band resulted from referencing and reproduced the baseline precision in this experiment).

Thus it was shown that a catalyst activity for a particular reaction can be detected fully automatically and can be optimized.

Claims

1. A process for investigation of chemical reactions in the presence of potentially catalytic substances, in which the reactions are conducted in parallel in reactors, which is characterized by the fact that the reactions are carried out in miniaturized reactors and the reaction mixture is analyzed according to kind and amount during the reaction time.

2. A process as in Claim 1, which is characterized by the fact that the reaction educts are supplied continuously to the reactors and the products are removed continuously from the reactors.

3. A process as in Claim 1 or 2, which is characterized by the fact that the reactions are carried out at different temperatures, preferably at temperatures from the range starting with room temperature up to 600°C inclusive or at various pressures, preferably at absolute pressures 10^{-3} to 10^{3} bar, especially preferably from 10^{-2} to 200 bar.

4. A process as in one or more of Claims 1 to 3, which is characterized by the fact that the potential catalysts are heterogeneous or homogeneous catalysts.

5. A process as in Claim 4, which is characterized by the fact that one uses a catalyst quantity <10 mg, preferably <1 mg, per reactor.

6. A process as in one or more of Claims 1 to 5, which is characterized by the fact that the reaction mixture or the

reaction products are spectroscopically analyzed according to kind and amount of constituents, preferably with IR spectroscopy.

7. A process as in one or more of Claims 1 to 6, which is characterized by the fact that the reactions are carried out in more than 20, preferably more than 40, especially preferably more than 100 reactors.

8. A process as in one or more of Claims 1 to 6, which is characterized by the fact that reactions of homogeneous or heterogeneous catalysis with liquid or gaseous educts or products are investigated.

9. A process as in Claim 6, which is characterized by the fact that the spectroscopic analysis is carried out simultaneously in all of the reactors, by using a corresponding number of analyzers, or that the spectroscopic analysis is carried out in the reactors one after the other, by directing an analysis beam with the aid of a deflector device successively onto the individual reactors or by bringing the reactors successively into the analysis beam with the aid of a rotation device.

10. A process as in one or more of Claims 1 to 9, which is characterized by the fact that one uses educts that are at least partly labeled with isotopes, preferably with deuterium or heavy oxygen or heavy carbon.

11. A process as in one or more of Claims 1 to 10, which is characterized by the fact that various educt mixtures are supplied to individual reactors or groups of connected reactors.

12. A device, especially for carrying the process in accordance with Claim 1, where the device has several reactors connected in parallel, which are provided with supply and discharge connections, which is characterized by the fact that

the reactors are miniaturized, with a volume from the range of 0.001 cm^3 to 1 cm^3.

13. A device as in Claim 12, which is characterized by the fact that the reactors are arranged in the form of a block, preferably cuboid or cubic.

14. A device as in Claim 12 or 13, which is characterized by the fact that the supply connections or the discharge connections or the reactors are at least partly transparent for the analysis beam, preferably for infrared, laser or UV light.

15. A device as in one or more of Claims 12 to 14, which is characterized by the fact that the reactors are arranged in a cuboid metal block, which is provided with heating elements and/or temperature measurement points.

16. A device as in one or more of Claims 12 to 15, which is characterized by the fact that the device is provided with rotation devices, preferably with step motors.

17. A device as in one or more of Claims 12 to 16, which is characterized by the fact that the device has more than 20, preferably more than 40, especially preferably more than 100, really especially preferably more than 200 reactors.

18. A device as in one or more of Claims 12 to 17, which is characterized by the fact that at least one reactor is provided with an ATR crystal, which enables spectroscopic contact to the reaction mixture.

19. A device as in Claim 15, which is characterized by the fact that the reactors are arranged in one plane parallel to one surface of the metal block, that the supply and discharge connections are arranged at least sectionally perpendicular to this plane, that a spacer, which has drillings through which the reactors or the connections can be lengthened, is affixed on the

surface, that the metal block and the spacer have cuvette drillings and that windows transparent for the analysis beam that seal the cuvette drillings from the environment are installed on the spacer plates.

20. A device as in one or more of Claims 12 to 19, which is characterized by the fact that the reactors contain catalysts, preferably with a weight less than 10 mg per reactor, especially preferably with a weight less than 1 mg per reaction.

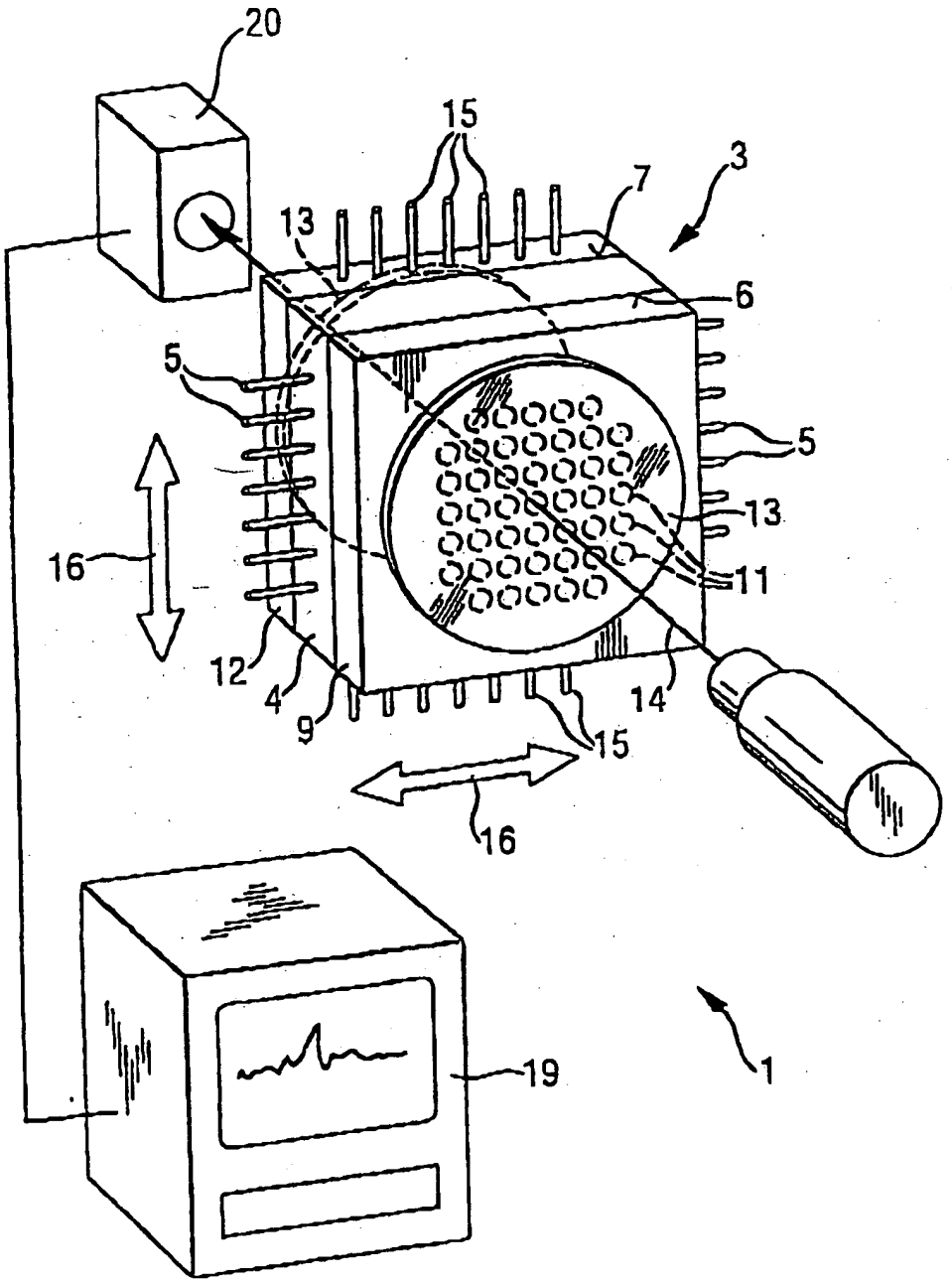

Figure 1

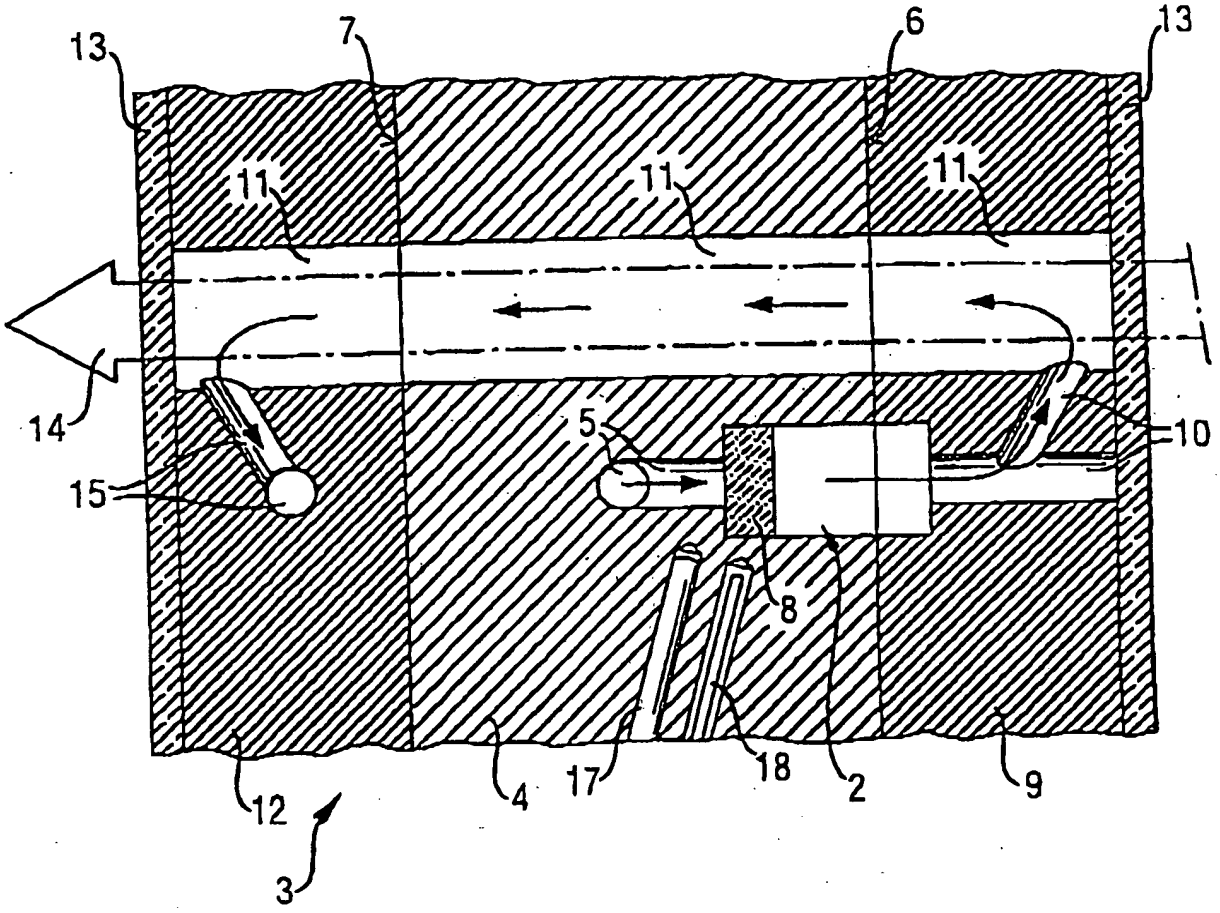

Figure 2

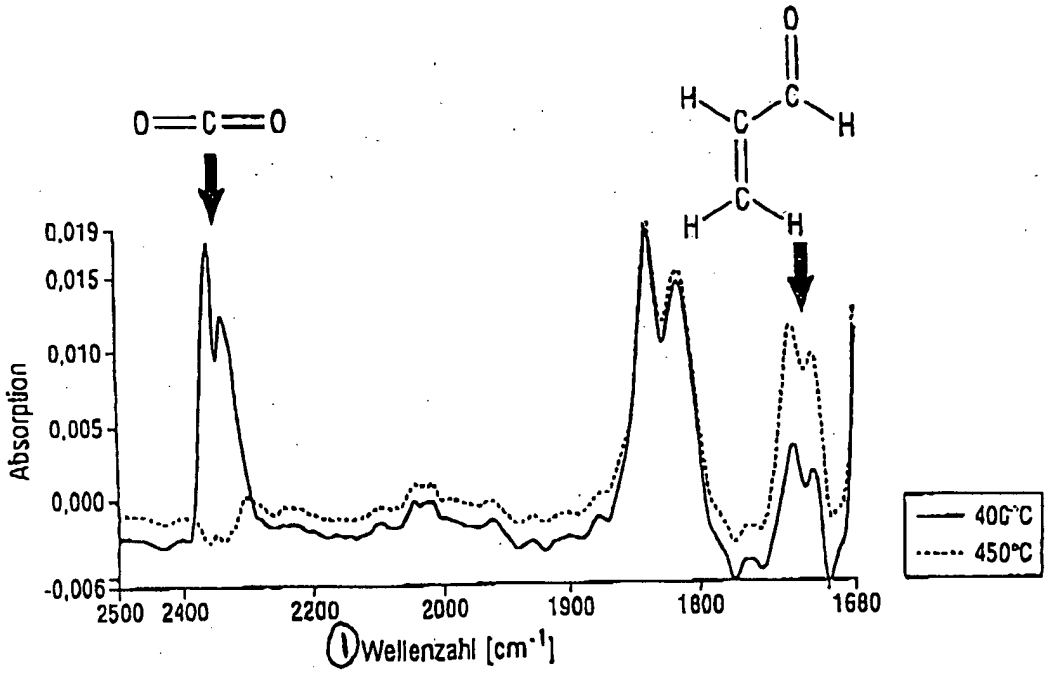

Figure 3: Screening and optimization of catalysts by online IR gas analysis in parallel reactors

Key: 1 Wave number